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From the INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(date/month/year)* 24 February 2005(24-02-2005)

Applicant's or agent's file reference
85128-1203

FOR FURTHER ACTION
See paragraph 2 below

International application no
PCT/CA2004/001698

International filing date *(date/month/year)*)
27 September 2004 (27-09-2004)

Priority date *(date/month/year)*
25 September 2003 (25-09-2003)

International Patent Classification (IPC) or both national classification and IPC
IPC 7: A61K 38/27; A61K 47/30; A61P 5/06

Applicant CANGENE CORPORATION ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[X]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
Commissioner of Patents
Canadian Patent Office
Box PCT, Ottawa/Gatineau K1A 0C9

Facsimile No. (819) 953-9538

Authorized officer
Nicole Harris (819) 997-4541

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language which it was filed, unless otherwise indicated under this item.

[ ] This opinion has been established on the basis of a translation from the original language into the following language __, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

a. type of material

[ ] a sequence listing

[ ] table(s) related to the sequence listing

b. format of material

[ ] in written format

[ ] in computer readable from

c. time of filing/furnishing

[ ] contained in the international application as filed.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority for the purposes of search.

3.[ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

Remarks: Claims 13-14 are directed towards methods of medical treatment of a human or animal which do not require examination under Rule 67.1 (iv) of the PCT. However, a written opinion with regards to novelty, inventive step and industrial applicability has been established based on the use of the formulations.

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Box No. IV **Lack of unity of invention**

1 [ ] In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has :

[ ] paid additional fees

[ ] paid additional fees under protest

[ ] not paid additional fees

2 [ ] This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3 This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

[X] complied with

[ ] not complied with for the following reasons :

4 Consequently, this opinion has been established in respect of the following parts of the international application :

[X] all parts

[ ] the parts relating to claims Nos. ____

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Box No. V reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-15	YES
	Claims		NO
Inventive step (IS)	Claims	3, 7 and 13-15	YES
	Claims	1, 2, 4-6 and 8-12	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations :

D1: US6011011 (PHARMACIA & UPJOHN COMPANY, Hageman MJ.) 4 January 2000

D2: CA2378949 (GRANDIS BIOTECH GMBH, Siebold B. et al.) 18 January 2001

D3: KATAKAM M. et al., "Use of Poloxamer Polymers to Stabilize Recombinant Human Growth Hormone Against various Processing Stresses", PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY, May 1997, vol. 2(2), pages 143-149

D1 discloses growth hormone formulations containing polyethylene glycol (PEG).

D2 discloses liquid growth hormone formulations comprising human growth hormone (hGH), mannitol, Pluronic F-86, and benzyl alcohol in phosphate buffer of pH 6.15-7.4, which are stable at 2-8 °C for storage greater than 6 months.

D3 discloses growth hormone formulations comprising hGH and Poloxamer 407, which stabilize the hGH against interfacial and thermal stress.

The problem to be solved by the present invention is to provide an aqueous growth hormone formulation that is stable over a long period of time.

D2 is the closest prior art, which provides stabilized growth hormone formulations, however, Pluronic F-86 is used in place of the PEG in the formulations of the instant application. Claims 1-15 differ from the growth hormone formulations of D1-D3. Therefore, claims 1-15 seem to meet the requirements of Article 33(2) of the PCT with respect to novelty.

D2 discloses liquid growth hormone formulations comprising hGH, mannitol, Pluronic F-86, and benzyl alcohol in phosphate buffer of pH 6.15-7.4, which are stable at 2-8 °C for storage greater than 6 months. Both D1 and D3 disclose alternative agents , PEG and Poloxamer, respectively, for stabilizing hGH formulations. It would be obvious to someone skilled in the art having read D2, armed with the knowledge that both PEG and Poloxamer are stabilizing pharmaceutical agents, to substitute PEG in place of Pluronic F-86 in the formulations of D2, to provide a PEG stabilized hGH formulation, since the only requirement of the instant formulations is that PEG is included in "an effective amount". As such claims 1, 2, 4-6 and 8-12 do not involve an inventive step (Article 33(3) of the PCT). Claims 3, 7 and 13-15, specifically define the concentration of PEG in the hGH formulations which can not readily be implied from D1-D3 and therefore claims 3, 7 and 13-15 do involve an inventive step (Article 33(3) of the PCT).

The subject matter of claims 1-15 is considered to be industrially applicable (Article 33(4) of the PCT). Certain contracting states of the PCT do not recognize the subject-matter of claims 13 and 14, methods of medical treatment, as industrially applicable. These states may however allow claims to a known formulation for a first medical use and the use of such formulations for the manufacture of a medicament for a new medical treatment. An opinion based on the industrial applicability of claims 13-14 has been established based on the use of said formulations.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 6 and 7 do not comply with Rule 6.4(b) of the *Regulations Under the* PCT which states that "any dependent claim shall be construed as including all the limitations contained in the claim to which it refers". Claims 6 and 7 ultimately depend on claims 2 and 3, respectively. Claim 2 further defines the growth hormone formulation of claim 1 by defining the polyethylene glycol as "PEG 1450 to PEG 20000" and claim 3 further defines the growth hormone formulation of claim 1 by defining the polyethylene glycol concentration in the range of "5 mg/ml to 50 mg/ml". The limitations on the growth hormone formulations of claims 6 and 7 have previously been defined in claims 2 and 3, making these claims redundant.